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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,909	11/04/2003	John R. Erbey II	CV06093	7785

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PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
HUYNH, CARLIC K	
ART UNIT	**PAPER NUMBER**
1617	
MAIL DATE	**DELIVERY MODE**
08/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,909	ERBEY ET AL.	
	Examiner	Art Unit	
	Carlic K. Huynh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 11-26* is/are pending in the application.

4a) Of the above claim(s) *24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 11-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks filed on June 8, 2007 is acknowledged.

Status of the Claims

1. Claims 1-3 and 11-26 are pending. Claims 4-10 have been cancelled in a Preliminary Amendment filed on March 21, 2005. Claims 25-26 have been withdrawn in a reply to a restriction requirement filed on November 28, 2006. Accordingly, claims 1-3 and 11-24 are considered herewith.

2. Claim 24 has been withdrawn because it is directed to a method of treating rheumatoid arthritis. It is noted Applicants have elected multiple sclerosis as a species of an autoimmune disorder in a reply to a restriction requirement filed on November 28, 2006. Thus claim 24 has been withdrawn. Accordingly, claims 1-3 and 11-23 are considered herewith.

Response to Arguments

Applicants' have cancelled claims 4-10. Claims 24-26 have been withdrawn.

3. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on June 8, 2007, with respect to "Rejections under 35 U.S.C. § 112, 1st paragraph" to claims 1-3 and 11-24 have been fully considered and are persuasive. The amended claims 1-3 and 11-24 have corrected the enablement rejection to "preventing an autoimmune disorder" by omitting "preventing an autoimmune disorder". Thus, the Rejections under 35 U.S.C. § 112, 1st paragraph to claims 1-3 and 11-24 have been withdrawn in light of the amendments.

4. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on June 8, 2007, with respect to "Rejections under 35 U.S.C. § 112, 2nd paragraph" to claim 3 have been fully considered and are persuasive. The compound represented for Formula (II) does indeed meet the limitations of the compound of Formula (I). Thus, the Rejections under 35 U.S.C. § 112, 2nd paragraph to claim 3 have been withdrawn in light of the amendments.

5. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on June 8, 2007, with respect to "Rejections under 35 U.S.C. § 102" to claims 1-3, 12-17, and 20-24 has been fully considered and are persuasive. The Liu et al. (US 6,569,879) reference is not a 102(b) reference but rather a 102(e) reference. Furthermore, Liu et al. does not specifically teach a method of treating multiple sclerosis comprising administering ezetimibe. Thus, the Rejections under 35 U.S.C. § 102(a) to claims 1-3, 12-17, and 20-24 have been withdrawn in light of the amendments.

6. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on June 8, 2007, with respect to "Rejections under 35 U.S.C. § 103" to claims 11 and 18-19 has been fully considered and are persuasive in part. The Vaccaro et al. reference (5,656,624) does not teach the compound of Formula (I). Thus, the Rejections under 35 U.S.C. § 103 to claims 11 and 18-19 have been withdrawn, in part, in light of the amendments. See new ground(s) of rejection below.

7. Applicant's arguments, see "Amendment-After Non-Final Rejection" filed on June 8, 2007, with respect to "Double Patenting" to claims 1-3, 11, 17-21, and 24 has been fully considered and are persuasive. Furthermore, a Terminal Disclaimer has been filed on June 8,

2007 on the Fine et al. application (10/701,244). Thus, the Double Patenting Rejections to claims 1-3, 11, 17-21, and 24 have been withdrawn in light of the amendments.

8. Applicant's arguments with respect to claims 1-3 and 11-24 have been considered but are moot in view of the new ground(s) of rejection. The following new ground(s) of rejection to the amended claims 1-3 and 11-23 are used herewith.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-3 and 11-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating arthritis and ulcerative colitis, does not reasonably provide enablement for treating any autoimmune disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:
(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the

amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). ***Nature of the Invention***:

The rejected claim(s) is/are drawn to an invention which pertains to (1) a method of treating an autoimmune disorder comprising administering a sterol absorption inhibitor of Formula (I) and (2) a method of treating an autoimmune disorder comprising administering a sterol absorption inhibitor of Formula (II).

(2). ***State of the Prior Art***:

The skilled artisan would view that the treatment of a vast array of any autoimmune disorders, is highly unlikely.

(3). ***Relative Skill of Those in the Art***:

The relative skill of those in the art of autoimmune disorders is extremely high.

(4). ***Predictability of the Art***:

The treatment of a vast array of autoimmune disorders with a sterol absortion inhibitor of Formula (I) or Formula (II) is highly unpredictable. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and that physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Thus, the state of the art is highly unpredictable.

(5). ***Breadth of the Claims***:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass the administration of a sterol absorption inhibitor of Formula (I) or Formula (II) as a treatment for any autoimmune disorder.

(6). ***Direction or Guidance Presented***:

The guidance given by the specification as to the method for treatment of any autoimmune disorders comprising administrating a sterol absorption inhibitor of the instant invention is limited.

The disclosure of the methods of manufacturing a sterol absorption inhibitor of Formula (II) of the instant invention is adequate (pages 48-51, example 1). The disclosure of the method for treating experimental arthritis comprising administrating a sterol absorption inhibitor of Formula (II) of the instant invention is adequate (pages 51-52, expample 2). The disclosure of the method for treating uclerative colitis comprising administrating a sterol absorption inhibitor of Formula (II) of the instant invention is adequate (pages 52-53, expample 3).

(7). ***Working Examples***:

The working examples in the specification show how to manufacture a sterol absorption inhibitor of Formula (II) (pages 48-51, example 1), how to evaluate the ability of a sterol absorption inhibitor of Formula (II) to treat experimental arthritis using an animal model of

rheumatoid arthritis (collagen-induced arthritis in DBA/1 or B10.RIII mice) (pages 51-52, example 2), and how to evaluate the ability of a sterol absorption inhibitor of Formula (II) to treat ulcerative colitis using a animal model of colitis (2,4,6-trinitrobenzene sulfonic acid-induced colitis in mice) (pages 52-53, example 3). Thus, the working examples show how to manufacture a sterol absorption inhibitor of Formula (II) and treat rheumatoid arthritis and ulcerative colitis with a sterol absorption inhibitor of Formula (II), not how to treat any autoimmune disorder.

Note that lack of a working example to treat any autoimmune disorder, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

(8). ***Quantity of Experimentation Necessary***:

The specification fails to provide sufficient support of an agent represented by Formula (I) or Formula (II) to treat any autoimmune disorder. As a result, one of skill in the art would be forced to perform an exhaustive search for the embodiments of any drugs having the function recited in the instant claim suitable to practice the claimed invention.

Therefore, in view of the Wands factors, e.g. the predictability of the art, the amount of direction or guidence, and the lack of working examples discussed above, a person of skill in the art would not be able to fully practice the instant invention without ***undue experimentation***.

Claim Rejections - 35 USC § 103

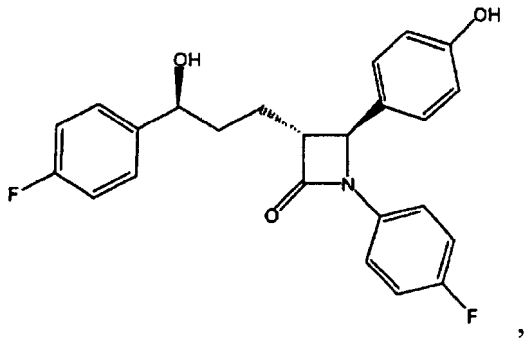
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-3 and 11-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (US 2002/0049222) as evidenced by van Heek et al. (British Journal of Pharmacology, 2001, Vol. 134, pp. 409-417) in view of Somers (US 6,147,250).

Yang et al. teach a method for treating conditions associated with inflammation, including rheumatoid arthritis and multiple sclerosis comprising administering modulators of chemokine receptor activity (abstract; and page 9, paragraphs [0357]-[0358]). The pharmaceutical compositions of the present invention include those that contain one or more active ingredients, in addition to a compound of the present invention (page 11, paragraph [0371]). The other active ingredients may be ezetimibe, HMG-CoA reductase inhibitors (e.g. simivastatin and atorvastatin), non-steroidal anti-inflamatory agents, and cyclooxygenase-2 (COX-2) inhibitors (page 11, paragraph [0372]). Yang et al. further teach when using the other active agents, such other drugs may be administered, by a route and in an amount commonly used therefor (page 11, paragraph [0371]).

As evidenced by van Heek, ezetimibe has a chemical structure of,



(page 410, figure 1).

Yang et al. do not teach sterol absorption inhibitors that disrupt lipid raft formation of leukocytes.

Somers teaches that HMG-CoA reductase inhibitors lower low density lipoprotein, LDL, levels as well as inhibit the expression of vascular cell adhesion molecule-1, VCAM-1 (column 5, lines 10-14 and column 7, lines 12-14).

Accordingly, absence the showing of unexpected results, it would have been obvious to employ the sterol absorption inhibitor of Yang et al. to disrupt the cell membrane organization of leukocytes and affect adhesion molecule function because the compounds of Somers are HMG-CoA reductase inhibitors and according to Somers, HMG-CoA reductase inhibitors inhibit adhesion molecule function in leukocytes.

The motivation to combine the sterol absorption inhibitors of Yang et al. to the compounds Somers is that the compounds of Somers are HMG-CoA reductase inhibitors and that such HMG-CoA reductase inhibitors inhibit adhesion molecule function in leukocytes.

Regarding the subject has rheumatoid arthritis and other agent as recited in claim 23, it is noted that Yang et al. teach a method of treating inflammatory conditions such as rheumatoid

arthritis comprising administering other agents such as cyclooxygenase-2 inhibitors as well as compounds of the present invention (page 11, paragraphs [0371]-[0372]). It would be obvious that the subject has rheumatoid arthritis because the teachings of Yang et al. may also include combinational therapy with cyclooxygenase-2 inhibitors that are used to treat inflammatory conditions.

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S. Wang

SHENGJUN WANG
PRIMARY EXAMINER

ckh